

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>29342/36206</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/ 11129</b>	International filing date (day/month/year) <b>26/04/2000</b>	(Earliest) Priority Date (day/month/year) <b>30/04/1999</b>
Applicant <b>LILLY ICOS LLC et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

**COMPOSITIONS COMPRISING PHOSPHODIESTERASE INHIBITORS FOR THE TREATMENT OF SEXUAL DISFUNCTION**

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A61K31/4985 A61P15/10

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 03675 A (GLAXO WELLCOME LAB SA ; DAUGAN ALAIN CLAUDE MARIE (FR)) 6 February 1997 (1997-02-06) page 3, line 11,12 page 3, line 24,25 page 5, line 4-11 claims; examples 1,3	1-19
P, X	WO 99 59584 A (ESTOK THOMAS MARK ; SCHERING CORP (US)) 25 November 1999 (1999-11-25) page 4, last paragraph page 42, line 11,12 page 61, line 20,21 claim 20	1-19

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

21 November 2000

Date of mailing of the international search report

28/11/2000

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 19978 A (GLAXO LAB SA ;DAUGAN ALAIN CLAUDE MARIE (FR)) 27 July 1995 (1995-07-27) cited in the application page 8, line 5-15; example 78 page 80, line 21,22 page 80, last paragraph claims 10,12,14 ---	1-12
P,X	DATABASE WPI Section Ch, Week 200029 Derwent Publications Ltd., London, GB; Class B02, AN 2000-339026 XP002152606 & WO 00 20033 A (EISAI CO LTD), 13 April 2000 (2000-04-13) abstract ---	1-12
A	ISRAEL M: "VIAGRA: THE FIRST ORAL TREATMENT FOR IMPOTENCE" PHARMACEUTICAL JOURNAL, PHARMACEUTICAL SOCIETY, LONDON, GB, vol. 261, 1 August 1998 (1998-08-01), pages 164-165, XP000919343 ISSN: 0031-6873 page 164, column 1-2 ---	1-19
A	GOLDENBERG M M: "SAFETY AND EFFICACY OF SILDENAFIL CITRATE IN THE TREATMENT OF MALE ERECTILE DYSFUNCTION" CLINICAL THERAPEUTICS, US, EXCERPTA MEDICA, PRINCETON, NJ, vol. 20, no. 6, 1998, pages 1033-1048, XP000853855 ISSN: 0149-2918 page 1041, column 1 -page 1042, column 1 -----	1-19

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/11129

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 13-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/11129

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9703675	A	06-02-1997	AU 704955 B	13-05-1999
			AU 6419196 A	18-02-1997
			BR 9609758 A	26-01-1999
			CA 2226784 A	06-02-1997
			CN 1195290 A	07-10-1998
			CZ 9800033 A	13-05-1998
			EP 0839040 A	06-05-1998
			HU 9900065 A	28-05-1999
			JP 11509221 T	17-08-1999
			NO 980153 A	10-03-1998
			PL 324495 A	25-05-1998
			SK 3998 A	08-07-1998
			US 6140329 A	31-10-2000
WO 9959584	A	25-11-1999	AU 4068599 A	06-12-1999
WO 9519978	A	27-07-1995	AP 556 A	07-11-1996
			AT 169018 T	15-08-1998
			AU 689205 B	26-03-1998
			AU 1574895 A	08-08-1995
			AU 707055 B	01-07-1999
			AU 7391298 A	20-08-1998
			BG 62733 B	30-06-2000
			BG 100727 A	28-02-1997
			BR 9506559 A	28-10-1997
			CA 2181377 A	27-07-1995
			CN 1143963 A, B	26-02-1997
			CZ 9602116 A	11-06-1997
			DE 69503753 D	03-09-1998
			DE 69503753 T	21-01-1999
			DK 740668 T	03-05-1999
			EP 0740668 A	06-11-1996
			ES 2122543 T	16-12-1998
			FI 962927 A	19-07-1996
			HR 950023 A	30-04-1998
			HU 74943 A	28-03-1997
			IL 112384 A	16-08-1998
			JP 9508113 T	19-08-1997
			LV 11690 A	20-02-1997
			LV 11690 B	20-06-1997
			NO 963015 A	09-09-1996
			NZ 279199 A	26-01-1998
			PL 315559 A	12-11-1996
			RU 2142463 C	10-12-1999
			SG 49184 A	18-05-1998
			SI 740668 T	28-02-1999
			SK 94096 A	09-04-1997
			US 6025494 A	15-02-2000
			US 6127542 A	03-10-2000
			US 5859006 A	12-01-1999
			ZA 9500424 A	27-09-1995
WO 0020033	A	13-04-2000	JP 2000178204 A	27-06-2000
			JP 2000191518 A	11-07-2000

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>29342/36206</b>	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. <b>PCT/US00/11129</b>	International filing date ( <i>day/month/year</i> ) <b>26/04/2000</b>	Priority date ( <i>day/month/year</i> ) <b>30/04/1999</b>	
International Patent Classification (IPC) or national classification and IPC <b>A61K31/00</b>			
Applicant <b>LILLY ICOS LLC et al.</b>			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  <b>02/11/2000</b>	Date of completion of this report  <b>25.09.2001</b>
Name and mailing address of the international preliminary examining authority:   <b>European Patent Office</b> <b>D-80298 Munich</b> <b>Tel. +49 89 2399 - 0 Tx: 523656 epmu d</b> <b>Fax: +49 89 2399 - 4465</b>	Authorized officer  <b>Veronese, A</b>  Telephone No. <b>+49 89 2399 7824</b>



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/11129

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-32 as originally filed

**Claims, No.:**

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/11129

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 13-17 (IA).

because:

☒ the said international application, or the said claims Nos. 13-17 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

### V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-19
	No: Claims
Inventive step (IS)	Yes: Claims
	No: Claims 1-19
Industrial applicability (IA)	Yes: Claims 1-12,18,19



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/11129

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No:      Claims

2. Citations and explanations  
**see separate sheet**

**VI.      Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**Re Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability.

Claims 13-17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT). However, although not required under the provisions of the PCT, an opinion will be given with respect to novelty and inventive step.

**Re Item V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

**INVENTIVE STEP**

Reference is made to the following documents:

D1: WO 97 03675 A (GLAXO WELLCOME LAB SA ;DAUGAN ALAIN CLAUDE MARIE (FR)) 6 February 1997 (1997-02-06)

D2: ISRAEL M: 'VIAGRA: THE FIRST ORAL TREATMENT FOR IMPOTENCE' PHARMACEUTICAL JOURNAL, PHARMACEUTICAL SOCIETY, LONDON, GB, vol. 261, 1 August 1998 (1998-08-01), pages 164-165, XP000919343 ISSN: 0031-6873

D1, see page 5 lines 4-14, example 1 (compound A) at page 10, the pharmaceutical formulations at pages 12-16 and claim 2 disclose the use of pharmaceutical unit dosages comprising the PDE5 inhibitor (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)-pyrazino [2',1':6,1] pyrido [3,4-b] indole-1,4-dione (Compound I) for the treatment of erectile dysfunctions. Compositions comprising 50 mg of compound I are shown and concentration ranges from 0.2 to 400 mg are indicated as suitable for oral administration. Compositions in the claimed range of 1 to 20 mg are therefore also considered to be implicitly disclosed.

If a novelty objection could be overcome, the selection of pharmaceutical unit dosages comprising 1 to 20 mg of Compound I as in the present invention can not however be considered to involve an inventive step.

The routine experimentation to optimise the required amounts of ingredients of known compositions for a known use falls within the normal capacity of the average skilled person. Even if the claimed compositions provide some benefits when compared to the compositions of the prior art, the experimental data reported in the present application are not characterized by any new or surprising effect.

Furthermore, for the patient treatment it is not the "unit dose" which is important to provide a certain medical effect, but the dose which is practically administered. For example two tablets or half tablet could be administered to the patient to adjust the dosage and obtain a certain effect.

The IPEA is therefore of the opinion that the subject-matter underlying claims 1-11, 13- 19 does not involve an inventive step in the sense of Art. 33(3) PCT.

Also claim 12, claiming the use of the PDE5 diesterase inhibitor I, for the treatment of sexual dysfunctions in woman is not considered to involve an inventive step in view of document D2, which discloses the use of PDE5 inhibitor VIAGRA for the treatment of sexual dysfunctions in females, see page 165, column 2.

#### **INDUSTRIAL APPLICATION**

For the assessment of the present claims 13-17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

#### **Re Item VI**

Certain documents cited (Rule 70.10)

WO9959584, which has been disregarded in writing the present Report, could become relevant for the assessment of novelty under some patent law systems. Priorities have not been checked.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/11129

Application No  
Patent No

Publication date  
(day/month/year)

Filing date  
(day/month/year)

Priority date (valid claim)  
(day/month/year)

WO9959584

25 November 1999 17 May 1999

20 May 1998

**Re Item VIII**

Certain observations on the international application

Claim 9 defines the subject-matter to be protected by way of the biological mechanism underlying the action of the disclosed compounds. This expression does not specify specific diseases recognized in the art to which the invention pertains and is not considered to fulfill the requirements of Art 6 PCT. The claim has been therefore examined under the assumption that the conditions indicated in claims 10-12 are intended.

The relative term "about" used in claims 1-6, 13-19 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

Claim 18 does not seem to define any additional subject matter and therefore does not comply with the requirements of conciseness of Art. 6 PCT.